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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,521	06/24/2003	David Edwin Thurston	065435-9027	2183

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MICHAEL BEST & FRIEDRICH LLP
ONE SOUTH PINCKNEY STREET
P O BOX 1806
MADISON, WI 53701

EXAMINER

EPPERSON, JON D

ART UNIT	PAPER NUMBER
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1639

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/602,521	Applicant(s) THURSTON ET AL.	
	Examiner Jon D. Epperson	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-64 is/are rejected.
- 7) ☒ Claim(s) 39 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 June 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/763,768.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>see attached</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants response filed December 29, 2006 is acknowledged

Status of the Claims

2. Claims 39-64 are currently pending. All previous restriction and/or election of species requirements are hereby withdrawn. Therefore, claims 39-64 are examined on the merits.

Information Disclosure Statement

3. The information disclosure statements filed November 13, 2000, March 10, 2005, fail, in part, to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because numerous publication(s) cited therein, lack titles (e.g., Althuis et al., Arima et al., etc), a necessary element for consideration (e.g., see marked up copies). While the other patent and other publications cited therein, and supplied, therewith, have been considered as to the merits, the above cited publications have not. Applicant is advised that the date of any re-submission of these citations contained in this information disclosure statement or the submission of the missing element – their publication dates – will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPE § 609 C(1).

4. The references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the form is attached to this Office Action (e.g., 11/13/00; 3/10/05; 4/26/06; 2/14/07).

Specification

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Objections to the Claims

6. Claim 39 is objected to because of the following informalities:
- A. Claim 39 uses the word “and” twice in a row in the last two lines of the claim. Correction is requested.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 39-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For ***claim 39, 51-58, and 61-63***, the phrase “and there is optionally a double bond between C1 and C2 or C2 and C3” is vague and indefinite because it is unclear which carbons are being referring to? Neither formula (XV) nor any of the side groups for R₂ and R₃ “number” their carbon atoms as C1, C2, C3, etc. Applicants are requested to clarify and/or correct. Therefore, claim 39, 51-58, 61-63 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

B. For ***claims 39, 40, 51-58, and 61-63***, the phrase “up to 12 carbon atoms” when

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used in conjunction with various organic groups like “aralkyl” and “aryl” is vague and indefinite. For example, up to includes “zero” as a lower limit (see *In re Mochel*, 470 F.2d 638, 176 U.S.P.Q. 195 (C.C.P.A. 1974) (“As this Court has held, the phrase “up to” ... includes zero as the lower limit. *Arness v. Franks*, 31 CCPA 737, 138 F.2d 213, 59 USPQ 154 (1943); accord, *In re Egbert*, 49 CCPA 888, 298 F.2d 947, 132 USPQ 456 (1962)”) and thus it is unclear how you can have an aralkyl or aryl group at all with “zero” carbons? Compare, for example, to the definition for “R is an alkyl group having 1 to 10 carbon atoms” which is proper (i.e., it is not defined as “R is an alkyl group having 0 to 10 carbon atoms”). Likewise, it is unclear how an “aryl” group can be formed from “one” carbon where no conjugated double bonds exist. The same argument can be made for Applicants are requested to clarify and/or correct. Therefore, claims 39, 40, 51-58, 61-63 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

C. **Claim 63** recites the limitation "the formula XV" in line 1. There is insufficient antecedent basis for this limitation in the claim (e.g., compare to claim 39 which recited removes the word formula). Therefore, claim 63 and all dependent claims are rejected under 35 USC 112, second paragraph.

D. **Claim 64** is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. More specifically, claim 64 fails to recite any positive method for performing the desired screening step.

Claim Rejections - 35 USC § 112, first paragraph

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 39-64 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 “Written Description” Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

Applicants’ claims are directed to various libraries of pyrrolobenzodiazepines. Virtually an infinite number of libraries fall within the scope of the present claims because Applicants do not set forth any structural limitations for the “T” variables (i.e., T, T’, T”) in formulas (II), (III), (IV), (VI), (VII), (VIII), (X), (XI), (XII), (XIV), (XVI) (XV), etc. Furthermore, many of the R₁₋₁₁ variables are defined independently with a wide range of Markush members. In addition, no upper limit is placed on the variables “n”, “m”, “q”, “p”, etc. (e.g., $n \rightarrow \infty$). That is, Applicants do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the T-groups. Likewise, all the dependent claims similarly fail to limit both n and T to anything less than an infinite number of possibilities.

In contrast, Applicants’ specification provides only a handful of examples with very limited substitutions at the R₆, R₇ and R₉ positions such as hydrogen, alkyl,

substituted alkyl (e.g., see also Figures 1-15 showing only hydrogen and CH₃O at the R_{9/6} and R₇ positions respectively). Furthermore, the R₂, R₃, positions contain only hydrogen (e.g., see figures 1-15). In addition only a limited number of combinatorial units are discussed including mainly peptides and peptide nucleic acids (e.g., see specification, pages 17-19).

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the claimed invention (e.g., see *In re Edwards*, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978); see also *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (CAFC 1991)). The “written description” requirement may be satisfied by using “such descriptive means as words, structures, figures, diagrams formulas, etc., that fully set forth the claimed invention” (e.g., see *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966). In the present case, Applicants describe only a handful of species (e.g., see above). In addition, when there is *substantial variation within the genus*, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05). Here, the variation within the genus would be enormous (see above). Virtually every class and subclass of molecules would fall within this claimed scope (e.g., biological polymers like peptides, non biological polymers like polyvinyl chloride, inorganic complexes, siloxanes, buckballs, etc. all fall within the scope of a “combinatorial” unit because any chemical group can be used in combinatorial synthesis).

Factors to be considered in determining whether there is sufficient evidence of

possession include “[1] the level of skill and knowledge in the art, [2] partial structure, [3] physical and/or chemical properties, [4] functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the [5] method of making the claimed invention” (e.g., see MPEP § 2163). Here, the level of skill in the art is high, but only with regard to a few of the species (e.g., peptides). For example, Lauf et al. state, “The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored” (e.g., see U.S. Patent Application Pub. No. 2004/0062911 A1, page 1, paragraph 4). Here, Applicants’ claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the “T” groups and, as a result, would read on the “largely unexplored” universe set forth in Lauf. In addition, Applicants provide no “partial structure” or “physicochemical properties” for the T group. Nor do Applicants set forth any structure/activity relationship for the combinatorial units. Finally, Applicants have not set forth any general method for making all of these compounds (e.g., siloxanes, fullerenes, etc.).

Thus, applicants have not demonstrated in “full, clear, concise, and exact terms” that they are in possession of the claimed libraries especially with regard to the T-groups. It is well settled that claiming only a result (e.g., compounds with T groups having the

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ability to function as combinatorial units) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result, far beyond those means actually discovered or contemplated by the inventor (e.g., compounds with small peptides at position R₆), so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217 ; *Siegel v. Watson*, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119.

9. Claim 64 is rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. All positive method steps, which are critical or essential to the practice of the invention, have not been included in the claim(s) and, therefore, is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Here, the claim omits a “contacting” step with a biological target. Furthermore, the claim omits a “detection” or “separation” step. These steps are essential to the claimed process for screening because an interaction between a target and a ligand is required before a screening process can occur and one must be able to identify said interaction once it does occur.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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10. Claims 39-51, 53 and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Thurston et al. (Thurston, et al. "Synthesis of a novel GC-specific covalent-binding DNA affinity-cleavage agent based on pyrrolobenzodiazepines" *Chem. Comm.* **1996**, 4, 563-565) (11/13/03 IDS).

For **claims 39-50 and 64**, Thurston et al. (see entire document) disclose a collection of pyrrolobenzodiazepines linked to Et₃EDTA (compound 14), EDTA (compound 14 after the hydrolysis step), or EDTA linked to metals like iron (compound 15), which anticipates the claimed invention (see Thurston et al., page 563, scheme 1). In this scenario, R_{2,3,6,9} = hydrogen; R₇ = OMe (i.e., OR group where R is C₁ carbon); A = O; Y = divalent -CH₂CH₂NH- (i.e., C₂ alkyl substituted with amino); X' is CO; n = 1 and H-T = Et₃EDTA or EDTA or EDTA complexed to Fe without the linking CO. Alternatively, Y = divalent -CH₂CH₂-; X' = NH; n = 1 and H-T = Et₃EDTA or EDTA or EDTA complexed to Fe with the linking CO. The OMe is also considered to be an "electron donating alkoxy" group because the lone pair of electrons on the oxygen can be delocalized into the ring. Note also that "AY" in this scenario is -OCH₂CH₂- (i.e., an alkoxy chain). The library also anticipates the claimed method set forth in claim 64 since no positive method steps are actually recited therein (e.g., see 35 U.S.C. § 112, second paragraph rejection above).

For **claim 51**, the variables are the same as set forth above except T' = NCH₂CH₂N(CH₂CO₂H/Et)CH₂ with or without the C=O and T'H/TH = CH₂CO₂Et or CH₂CO₂H. That is the EDTA, Et₃EDTA have simply been viewed in a different way to fit formula (VIII) as recited in the claim.

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For *claim 53*, the variables are the same as set forth above except T = CH₂N(CH₂CO₂H/Et) with or without the C=O; T'' = CH₂CH₂N; and T'H/T''H = CH₂CO₂Et or CH₂CO₂H. That is the EDTA, Et₃EDTA have simply been viewed in a different way to fit formula (XVI) as recited in the claim.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jon D. Epperson/
Primary Examiner, AU 1639